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EXAMINER	
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ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/605,708	GONG ET AL.	
	Examiner	Art Unit	
	Anoop Singh	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *17-19,22-28,33 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16, 20-21, 29-32 and 35-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/11/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on August 11, 2006, has been received and entered. Claims 1, 36 and 43 have been amended. Applicants have also added claim 42 which is generally directed to elected invention.

Election/Restrictions

Applicant's election of claims 1-16, 20-21, 29-32 and 35-41 in the reply filed on January 19, 2006 was acknowledged. Claim numbering as filed in instant application from 1-41 was used for restriction requirement. It is noted that applicants required further clarification on restriction requirement of patentably distinct invention. In this regard it was stated that Examiner required election between patentably distinct inventions of transgenic fish made by different promoter (restriction/election requirement, pp 2, section 4). Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different mode of operation, different functions or effect (MPEP § 806.04, MPEP §808.01). In the instant case the different polynucleotide, sequences represent unique and different promoter sequences with different inherent properties as demonstrated by a specific expression pattern in a specific cell type. Therefore, each transgenic fish comprising a different promoter would results in a material different genome in the transgenic fish. In addition, each promoter may result in specific and unique phenotype resulting in patentably distinct transgenic

fish. Page 2 section 4 clearly states, applicants are required to elect one promoter for prosecution on merit and it was emphasized that it is a restriction requirement not election of species. The applicants election to muscle specific promoter was acknowledged.

The requirement was deemed proper and was therefore made FINAL.

Accordingly, a method of providing transgenic fish to ornamental fish market by obtaining an ornamental transgenic fish comprising one or more fluorescent gene operably linked to muscle specific promoter such that it expresses the fluorescence upon exposure to one or more blue light and distributing said fish in ornamental fish market will be examined in the instant application.

Claims 17-19, 22-28 and 33-34 were withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction/election requirement in the reply filed on 1/19/2006.

Claims 1-16, 20-21, 29-32 and 35-42 are pending.

New-Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16, 20-21, 29-32 and 35-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118(a) states "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application". In the instant case, the recitation of limitation... "a transgenic fish comprising fluorescent genes positioned under the control of a promoter wherein transgenic fish expresses one or more fluorescent protein encoded by one or more fluorescence genes " (claims 1 and 36), is considered new matter. Applicants do not have support for distributing "a transgenic fish comprising one or more fluorescent gene under the control of any promoter" in the ornamental fish market, rather specification provides support only to a transgenic fish comprising fluorescent(s) gene under the control of tissue specific promoter resulting in a transgenic fish that expresses fluorescent gene at a sufficient level such that said transgenic fish shows fluorescence upon exposure to one or more blue, ultra or sun light fluorescent protein (see page 41-43 of the specification). It is emphasized that specification provides support directly to a transgenic fish comprising specifically fluorescent gene operably linked to a tissue specific promoter that expresses fluorescent gene at appropriate levels. Upon further review of the instant amended claims it is evident that these claims do not require transgenic fish to show any fluorescence, which is not contemplated by the specification

for providing these fish to ornamental fish market. In addition, these limitations of claims 1 and 36 also do not have any explicit support in the specification for providing these transgenic fish to ornamental fish market. It is noted that this section does not provide the specific conditions, nor what and how one determines an equivalent that would generically apply to the claimed invention.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph-written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981) teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time application was filed... If a claim is amended to include subject matter, limitation or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes, "When an amendment is filed in reply to an objection or rejection based on U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendment made to the disclosure".

To the extent the claimed compositions are not described in the instant disclosure, claims 1-16, 20-21, 29-32 and 35-42 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with

which it is most nearly connected, to make and/or use the invention, since the applicants disclosure do not teach a method of providing transgenic fish to ornamental fish market comprising obtaining any transgenic fish comprising fluorescent gene operably linked to any promoter, wherein fluorescence fish express fluorescence gene for distribution of said transgenic fish to ornamental fish market that is adequately described in the specification. In this case, it appears that the claims reflect transgenic fish comprising fluorescent gene under the control of any promoter, wherein said fish expresses fluorescent gene at a level that is not required to show any significant fluorescence upon exposure to light. As described before claims as amended recite providing a transgenic fish that would have no commercial value, the specification does not provide adequate guidance on determining what is included or excluded by the claims as amended and therefore an artisan of skill would require undue experimentation to practice or make and/or use the invention.

New Grounds of Claim Rejections– Necessitated by amendement-35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16, 20-21, 29-32 and 35-41 remain rejected under 35 U.S.C. 112, first paragraph and newly added claim 42 is also under 35 U.S.C. 112, first paragraph because the specification, while being enabling for a method of providing transgenic fish

to the ornamental fish market comprising the step of (a) obtaining a transgenic zebrafish comprising a chimeric fluorescent gene operably linked to a muscle specific promoter selected from the list consisting of (i) zebrafish muscle creatine kinase gene promoter (SEQ ID NO: 8) such that said transgenic fish expresses fluorescent protein encoded by fluorescent gene in muscle, (ii) zebrafish fast skeletal myosin light chain 2 gene promoter (SEQ ID NO: 22) such that said transgenic fish expresses fluorescent protein encoded by fluorescent gene in skeletal muscle; at a level sufficient such that said transgenic fish fluoresces upon exposure to one or more light and (b) distributing said fish to the ornamental fish market, does not reasonably provide enablement for using any promoter or any other species of transgenic fish. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In determining whether Applicant's claims are enabled, it must be found that one of skill in the art at the time of invention by applicant would not have had to perform "undue experimentation" to make and/or use the invention claimed. Such a determination is not a simple factual consideration, but is a conclusion reached by weighing at least eight factors as set forth in In re Wands, 858 F.2d at 737, 8 USPQ 1400, 2d at 1404. Such factors are: (1) The breadth of the claims; (2) The nature of the invention; (3) The state of the art; (4) The level of one of ordinary skill in the art; (5) The level of predictability in the art; (6) The amount of direction and guidance provided by Applicant; (7) The existence of working examples; and (8) The quantity of experimentation needed to make and/or use the invention.

These factors will be analyzed, in turn, to demonstrate that one of ordinary skill in the art would have had to perform "undue experimentation" to make and/or use the invention and therefore, applicant's claims are not enabled.

Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working example are not disclosed in the specification, therefore enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore, skepticism raised in enablement rejections are those raised in the art by artisan of expertise.

Claims 1-16, 20-21, 29-32 and 35-42 are broad in scope. The following paragraph will outline the full scope of the claims. Claimed invention recites a method of providing transgenic fish to the ornamental fish market by obtaining an ornamental transgenic fish. Thus, in the instant case transgenic fish comprising a fluorescent gene has been analyzed. Claims 1-16 encompass a method of providing transgenic fish by obtaining transgenic fish comprising one or more chimeric fluorescent genes operably linked to a promoter such that transgenic fish expresses one or more fluorescent gene upon exposure to one or more light. Subsequent claims limit the wavelength and fluorescent gene to specific light wavelength and genes. Claims 16, 20-21 recite tissue specific promoter subsequently limiting to zebrafish muscle creatine kinase gene and zebrafish myosin light chain 2 gene promoter. Claim 29 limits the method of claim 16 to include more than one fluorescent protein color. Claim 30 limits the expression of color in same tissue to affect an original color. Claim 31 limits the fluorescent gene of claim 30 to include GFP and BFP. Claim 32 limits the method of claim 29 to include more than

one fluorescent protein that are separately expressed in different tissues. Claims 36-41 limit the method of claim 1 to include stable transgenic fish line.

These claims encompass plurality of fish species and any promoter that would be used for expressing fluorescent gene in fish. The disclosure provided by the applicant, in view of prior art, must encompass a wide area of knowledge to a reasonably comprehensive extent. In other word each of those, aspect considered broad must be shown to a reasonable extent so that one of the ordinary skills in the art at the time of invention by applicant would be able to practice the invention without any undue burden being on such Artisan.

The specification broadly discloses role of transgenic fish in medical research and method of introducing foreign gene in fish (pp. 3). The invention is based in part to develop fluorescent transgenic ornamental fish using fluorescent gene construct. The specification generally describes use of different gene promoters that could express plurality of fluorescent gene in different tissue (pp 7). Pages 9-15 provide brief description of drawing. Pages 15-47 provide detailed description of the invention, preferred embodiment, gene construct and general method to prepare fluorescent transgenic fish and other techniques disclosed in the instant application. Remaining specification describes the specific example of the ornamental transgenic carrying characteristics similar to one described in this office action. Example 1: of specification teaches isolation of muscle specific and ubiquitously expressed zebrafish cDNA clones. Example 2 discloses isolation of four-zebrafish gene promoter. Example 3 describes generation of green fluorescent transgenic fish. "It is noted that specification itself states

that only two construct (2011 bp and 1338 bp) are capable of maintaining the high level of expression and highest expression was seen with only 2 -Kb promoter suggesting the importance of promoter region of 1338 bp to 2011 bp for conferring the highest promoter activity". Example IV discloses potential applications of fluorescent transgenic fish as ornamental fish.

The specification does not provide any specific guidance as to how transgenic fish in other species would be made. In fact, Applicant's examples only describe a transgenic zebrafish as claimed in the instant application. At the time of the invention, although many of the methods are routine, neither art of record nor the specification teaches how to practice the claimed invention for all different species of fish as recited in the claimed invention. It is noted that the specification as filed does not provide any specific information for practicing the claimed transgenic fish comprising fluorescent gene operably linked to any promoter. An artisan would have to carry out extensive experimentation to make and use the invention in other species with different promoters and such experimentation would have been undue because of the art of making ornamental transgenic fish using any promoter was unpredictable and specification fails to provide any guidance as to how the claimed method would have been practiced.

For example, Betancourt et al (Mol Mar Biol Biotechnol. 1993, 2(3): 181-8) state "elements from mammalian genes may not be properly recognized by the fish cellular machinery and in an unpredictable manner". It is noted that Betancourt et al suggest that vectors prepared to express foreign genes in transfected cultured fish cells and transgenic fish should preferably contain DNA sequences from fish genes or,

alternatively, those sequences from mammalian genes that have been previously proved to be compatible with the fish cellular machinery (abstract). It is not apparent how the instant method of providing fish to ornamental fish market contemplates obtaining transgenic fish comprising fluorescent gene operably linked to any promoter sequence derived from any source. Bearzotti et al. (J Biotechnology. 1992, 26(2-3): 315-325) also suggest that the translation and secretion machinery of fish cells can express efficiently foreign genes but that mammalian intron might be not processed properly in some cases. Higashijima et al (Dev Biol. 1997; 192(2): 289-99; IDS) describe factors that potentially affect the transgenic frequency or expression levels. Higashijima et al state that (i) expression levels of GFP in the injected embryo are not strongly correlated to transgenic frequency; (ii) a plasmid vector sequence placed upstream of the construct might reduce the expression levels of the reporter gene. The specification does not provide any guidance as to how would an artisan select any promoter to express any fluorescent gene at any site in any fish.

Furthermore, as amended instant claims do not require expression of fluorescence gene at a level sufficient so that they fluoresce upon exposure to light. Since instant transgenic fish is commercially viable in ornamental fish market because they fluoresce, thus instant claims as recited are not enabled because these transgenic fish may not even express fluorescent gene at sufficient level so that they fluoresce upon exposure to light. Therefore, at the time of the invention there was no evidence of expressing fluorescent gene at any site using any promoter in any fish and a method to obtain transgenic ornamental fish to provide in ornamental fish market would have been

unpredictable since a number of factors played role in the predictable expression of the transgene as shown by the art of record.

In conclusion, in view of breadth of the claims and absence of a strong showing by Applicant, in the way of specific guidance and direction, and/or working examples demonstrating the same, such invention as claimed by Applicant is not enabled for the claimed inventions. The specification and prior art do not teach a method of providing transgenic fish to an ornamental fish market comprising the step of obtaining an ornamental fish comprising any fluorescent gene operably linked to any promoter that expresses said gene and distributing said fish to the ornamental fish market. An artisan of skill would have required undue experimentation to practice the method as claimed because the art of using any promoter for gene expression in general in fish was unpredictable at the time of filing of this application as supported by the specification and observations in the art record.

Response to Arguments

Applicant's arguments filed August 11, 2006 have been fully considered but they are not persuasive. Applicants in their argument on pages 7-9 state that many different species of fish have now been genetically engineered and now the genetic engineering of fish is generally routine. Applicants cite several issued patents (5,998,698, 6,307,121 and 6,472,583) to assert that transgenic fish of different species to show are fully enabled.

In response, it is emphasized that instant claims are not directed to a method of making of transgenic fish. In fact independent claims 1 and 36 are directed to a method of providing a transgenic fish to ornamental fish marker by obtaining a any transgenic fish comprising a fluorescent gene operably linked to any promoter, wherein transgenic fish expresses fluorescent gene (emphasis added). It is noted that that cited references only provides a general method that are either capable of expressing heterologous lytic peptide or mutation detection. It is emphasized that the patentability of each patent application is examined in view of its own disclosure and merits depending on what is claimed. It is emphasized that a method for making transgenic fish for other purposes is not enabling disclosure and cannot be extrapolated to a very specific method for providing transgenic ornamental fish to ornamental fish market that requires a very specific transgenic fish that requires expression of fluorescent gene at sufficient levels such that transgenic fish fluoresces upon exposure to light as contemplated in instant application. Furthermore as amended instant claims further broaden the scope of previously rejected claims encompassing any transgenic fish comprising fluorescent gene and any promoter that expresses one or more fluorescent protein. It is emphasized that as amended these claims do not even require transgenic fish to express fluorescent gene at a level sufficient to fluoresce upon exposure to any light. As stated in previous office action prior art teach numerous factors that potentially affect the transgenic frequency or expression levels in transgenic fish including (i) expression levels not strongly correlated to transgenic frequency; (ii) placement of construct (Higashijima et al (Dev Biol. 1997; 192(2): 289-99; art of record). The intent is not to say

that transgenic fish of other species cannot be made rather art of making transgenic ornamental fish of different species for the distribution in ornamental fish market is unpredictable and dependent upon the expression level of fluorescent gene in different species. Furthermore, transgenics art generally recognizes that different promoter would have different expression levels that would be critical in determining whether a species of transgenic fish would fluoresces upon exposure to any light in order to be commercially relevant as required by independent claims. In the instant case, the methods presented by the working examples appeared to correlate more with tissue specific promoter that express fluorescent gene at level sufficient such that these fish fluoresces upon exposure to the light. Therefore, the specification does not enable to a method of providing transgenic ornamental fish to ornamental fish market commensurate with full scope of the claim as stated in previous office action dated 3/8/2006.

Applicants provide references of Kuo et al, Moss et al and Hackett et al to assert that abundance of non fish tissue specific and other promoters were routinely found operable in fish. Applicants also assert that Examiner cited references are old and support enablement. Applicants argue that the fact that something does not work as well "does not lead to the conclusion" that the present invention is not enabled for the preparation of any transgenic fish using any promoter (see page 9).

In response, Applicant's arguments have been fully considered but they are not persuasive. Applicant's again ague the fact that method of making transgenic fish using any promoter is enabled, however, contrary to the applicants argument the issue at

hand is not whether applicants are enabled for a method of making any transgenic fish with any promoter, rather issue is whether applicants are enabled for a method of providing a transgenic ornamental fish by obtaining a fish that expresses fluorescent gene at a level sufficient such that said fish fluoresces upon exposure to the light. Applicants agree to the fact all promoter may not work well in fish (see page 9), however argues "that does not lead to the conclusion the present invention is not enabled for the preparation of making transgenic ornamental fish". Examiner completely disagree and emphasize that transgenic ornamental fish to be distributed in the ornamental fish market require expression of fluorescent gene to sufficiently high level in order for fish to fluoresce upon exposure to light. It is noted that using any promoter that does not work or sub optimally work in fish will not express fluorescent gene at a sufficient level such that fish fluoresces upon exposure to the light. The specification teaches only two construct (2011 bp and 1338 bp) are capable of maintaining the high level of expression and highest expression was seen with only 2 -Kb promoter suggesting the importance of promoter region of 1338 bp to 2011 bp for conferring the highest promoter activity (supra). Furthermore, Applicants own specification describes that use of heterologous gene promoter from SV 40 and RSV and other promoters in studying zebrafish that shows expression pattern of a transgene in many case variable and unpredictable" (see page 6, 7 and 15 of the specification, paragraph 6 and also paragraph 28; emphasis added). It is emphasized that claims are not directed to a method of making transgenic fish rather they are directed to a method for providing commercially viable transgenic ornamental fish that fluoresces upon exposure to

different light. In light of the contemplation of the specification, it appeared that choice of promoter could greatly effect the levels of expression, therefore, at the time of filing of this application, method of providing transgenic ornamental fish using any promoter in any species of fish would have required undue experimentation to make and use of invention commensurate with full scope of the invention.

Withdrawn-Claim Rejections - 35 USC § 112

Claims 1-16, 29-32 and 35-41 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn since claims are directed to any promoter that is generally known in the art.

Withdrawn-Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-16, 20-21, 29-32, 35-41 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention are withdrawn in view of amendments to the independent claims 1 and 36.

Maintained-Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-8, 16 and 36-41 remain rejected under 35 U.S.C. 103(a) and newly added claim 42 is also rejected under 35 U.S.C. 103(a) as being unpatentable over Higashijima et al (Dev Biol. 1997; 192(2): 289-99, IDS) and Bryan et at (US Patent no. 6436682 8/20/2002, filing date, 6/30/ 2000, effective filing date 3/ 27/ 1998).

Higashijima et al teach generating transgenic zebrafish using a β-actin–GFP construct. Higashijima et al show GFP is expressed throughout the body of one line whereas other two transgenic lines showed identical spatial expression of GFP in muscle cells (pp 295, col. 1, para 2, Fig 4), demonstrating consistent expression of green fluorescence. It is also noted that Higashijima et al show stable transmission of GFP expression in three lines of F3 generation suggesting that transgene is stably

integrated into the genome of each line (pp 297, col. 1, para 1). It is also disclosed that fluorescence expression could be seen with FITC filter suggesting that fluorescent expression on fish could be best viewed at excitation wavelength of blue light (360-420 nm) (pp 292, col.2, para 2). However, Higashijima et al do not teach distributing the transgenic fish to the market.

Bryan et at teach a combinations containing a first composition containing a luciferase and a second composition containing one or more additional components of a bioluminescence-generating system for use to produce novelty items. These novelty items also include transgenic fish, particularly transgenic fish that express a luciferase (col. 8, line 16). It is noted that these novelty items are designed for entertainment, recreation and amusement including use of the item to attract attention (col. 8, lines 25-29). Bryan et al also disclose that such uses of the novelty item may in the place of normal or ordinary uses of such an item (col. 8, line 33). Thus, teachings of Bryan et al encompass displaying fluorescent fish at ornamental fish market. However, Bryan et al do not specifically teach obtaining ornamental transgenic fish comprising a promoter operably linked to a fluorescent gene.

It would have been obvious for one of ordinary skill in the art at the time of invention to modify the method of Higashijima by providing fluorescent transgenic fish as novelty item to ornamental fish market as described by Bryan. Higashijima et al had already disclosed a method for making fluorescence transgenic fish displaying green fluorescence in the muscle of the fish. In addition, Bryan et al had described that novelty items such as transgenic fish comprising fluorescent genes could be designed for

entertainment, recreation and amusement including use of the item to attract attention (col. 8, lines 25-29). The skilled artisan would have been motivated to modify the method of Higashijima to distribute transgenic fish as suggested by Bryan as novelty item.

One who would have practiced the invention would have had reasonable expectation of successfully obtaining a transgenic fish comprising fluorescent gene and distributing in the market because Higashijima already taught a method for making fluorescent transgenic fish and Bryan had taught fluorescent transgenic fish could be made for entertainment, recreation and amusement including use of the item to attract attention. One of ordinary skill in art would have been motivated to combine the teaching Higashijima and Bryan because a fluorescent transgenic fish comprising one or more fluorescent gene operably linked to a promoter would have provided fluorescent fish that would have attracted attention upon distribution of fluorescent transgenic fish as a novelty item in a place of normal or ordinary uses of such an item (pet store or ornamental fish market) as taught by Bryan.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

Response to Arguments

Applicant's arguments filed August 11, 2006 have been fully considered but they are not fully persuasive. Applicants in their argument on pages 14-19 state Applicants agree that if transgenic fish of Higashijima et al were to be sold at ornamental fish

market then such a sale would be covered by the pending claims. Applicants assert Bryan et al do not suggest sale of fluorescent fish in the market. Applicants argue that Bryan et al teach a wide variety of novelty item that mostly includes inanimate objects. Applicants state that transgenic fish is recited only in context of phrase fish food containing luceferins and particularly a transgenic fish expressing luciferase. Applicants then argue that Bryan is in fact describing fish food. Applicants also assert that even if one were to assume that Bryan et al would read by one of skill as teaching the feeding of luciferin to live luciferase transgenic fish there would still be no proper basis for maintaining obviousness rejection. Applicants point out differences in bioluminescence and fluorescence. Applicants assert that at best one of ordinary skill in the art would not be motivated to sell the fluorescent fish rather expected to sell bioluminescent fish in combination with bioluminescent substrate.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Examiner in part agree that Bryan et al do not teach explicitly teach an ornamental transgenic fish comprising a promoter operably linked to a fluorescent gene. The fact that if Bryan had disclosed a transgenic fish showing fluorescent gene, this would have not been an

obviousness type rejection rather Bryan would have anticipated the instantly claimed invention. It is noted that Bryan et al teach novelty items include transgenic fish, particularly transgenic fish that express a luciferase (col. 8, line 16-17, emphasis added). It is noted that these novelty items are designed for entertainment, recreation and amusement including use of the item to attract attention (supra). In fact, Bryan et al also contemplated expressing luciferase in host and animal cells (see column 7, lines 26-40). Thus, it is apparent that contrary to Applicants argument Bryan contemplates displaying a number of novelty items that could be displayed for entertainment and amusement including use of the item to attract attention such as transgenic fish that expresses luciferase (column 8, line 16, 26-27; supra). It is further noted that claims are directed to a method of providing transgenic ornamental fish to ornamental fish market. The reference of Bryan is included to demonstrate that fish emitting light or glowing because of bioluminescence or any other mechanism were considered novelty item for display. Applicants argument that an artisan would be motivated to provide bioluminescent fish not a fluorescent fish to the ornamental fish market is not persuasive. Since bioluminescence is defined as "emission of light from living organisms; *also* : the light so produced", while fluorescence is "luminescence that is caused by the absorption of radiation at one wavelength followed by nearly immediate re radiation usually at a different wavelength and that ceases almost at once when the incident radiation stops" (http://m-w.com/dictionary/). Thus, the light emitted by fluorescence would clearly also encompass light emitted by bioluminescent. Furthermore, the fact that the wide varieties of items emitting light were considered

items for display and their market value was solely dependent upon their ability to glow or show different colors. An artisan would have been sufficiently motivated to provide the transgenic fish showing color (emitting light) by any mechanism such as one disclosed by Higashijima et al to the ornamental fish market with reasonable expectation of success, since light emitting fish were already considered novelty item to attract attention as taught by Bryan.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

Maintained-Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-16, 20-21, 29-32 and 35-41 are also provisionally rejected on the ground of non statutory double patenting over claims 7-20 of co pending Application No. 09/913, 898. This is a provisional double patenting rejection since the conflicting claims have not yet been patented. The subject matter claimed in the instant application is fully disclosed in the referenced co pending application and would be covered by any patent granted on that co pending application since the referenced co pending application and the instant application are claiming common subject matter, because both sets of claims encompass providing transgenic ornamental fish to the ornamental fish market.
For example, claims 1-16, 20-21, 29-32 and 35-41 of instant application encompasses a method of providing transgenic fish to the ornamental fish market comprising one or more chimeric fluorescence gene under the control of a promoter such that transgenic fish expresses one or more fluorescence gene at sufficient level upon exposure to one or more light and distributing said fish to the ornamental fish market. Claims 2-15 limit the fluorescent gene to include plurality of gene. Claim 16 limit the promoter of claim 1 to include tissue specific promoter that is subsequently limited to include zebrafish muscle creatine kinase gene promoter and zebrafish myosin light chain 2-gene promoter. Claims 29-32 limit the method of claim 16 to include plurality of fluorescent gene under the control of tissue specific promoter. Claims 36-41 are directed to the method of claim 1 to include stable transgenic fish line.

Whereas, Claim 7 of the Patent application no 09/913, 898 is directed to a transgenic fish comprising a zebrafish muscle creatine kinase or MLC2 gene promoter operably linked to fluorescent gene such that it expresses the fluorescent gene in tissue

specific manner. Subsequent claims limit the transgenic fish of claim 7 to include promoter in germ cells and /or in somatic cell and that is capable of breeding with either transgenic fish or non transgenic fish to produce viable progeny and such progeny emit green fluorescence when the whole fish is exposed to plurality of light wavelength. Claim 19 define the transgenic fish of claim10 to ornamental fish for ornamental fish market. Thus, claims 7-20 of US Patent application no 09/913898 broadly encompasses all the recited claims 1-16, 20-21, 29-32 and 35-41 of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

It is noted that Applicants have not responded to the double patenting rejection. In absence of any argument, nonstatutory double patenting rejection is maintained for the reasons of the record.

No Claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anoop Singh whose telephone number is (571) 272-3306. The examiner can normally be reached on 9:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272- 0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anoop Singh, Ph.D.
Examiner, AU 1632

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